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08/971,172	11/14/1997	COREY S. GOODMAN		3769

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EXAMINER	
TURNER, SHARON L	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

AT

UNITED STATES DEPARTMENT OF COMMERCE
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Washington, D.C. 20231

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 38

Application Number: 08971172
Filing Date: 14 November 1997
Appellant(s): Goodman et al.

Richard Aron Osman
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief filed 02 July 2002 (hereinafter, the Brief).

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the

pending appeal is contained in the brief. Applicant's state that they are unaware of any related appeals or interferences. Therefore, it is presumed that there are none. The Board, however, may exercise its discretion to require an explicit statement as to the existence of any related appeals and interferences.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is substantially correct. However, it is noted that the first sentence of the paragraph states that the invention relates to diagnostic probes but in contrast to the assertion the claims are drawn to isolated polynucleotides, cells and a method of making a Robo polypeptide using the claimed polynucleotides. There are no diagnostic probe limitations within the claims.

(6) Issues

The appellant's statement of the issues in the brief is substantially correct. The changes are as follows:

Rejection of claim 104 under 35 USC, 112, first paragraph has been withdrawn. The rejection was resolved with respect to new matter based upon Appellant's reference to support at p. 4, line 19.

Rejection of claims 108-110 under 35 U.S.C. 102(a) has been withdrawn. The rejection was resolved based upon performance of an alignment with the newly designated residues of the Word document submitted in the after final amendment. The alignment shows 100% identity within the designated region of residues 1-3630 of the Word document and with residues 1-3630 of SEQ ID NO:7.

(7) Grouping of Claims

Appellant's brief includes a statement that the claims as noted at p. 3 of the brief do not stand or fall together and provides reasons within the Argument's section for such grouping as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

Seeger et al., "Mutations affecting growth cone guidance in Drosophila: genes necessary for guidance toward or away from the midline." Neuron, vol. 10, no. 3 (March 1993), pp. 409-426.

Strembl-11, Accession No. O01632, Wilson et al., cDNA sequence, 01 July 1997.

GenBank Accession No. U88183, Wilson et al., 14 February 1997.

GenBank Accession No. Z95705, Cahn et al., 25 May 1997

Sambrook et al., "Molecular Cloning." Cold Spring Harbor Labs, 1989, pp. 16.1-16.16.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 68-91 and 93-119 are rejected under 35 U.S.C. 101. This rejection is set forth in the prior Office Action of 3-27-01, Paper Nos. 24. As set forth therein, the specification discloses the amino acid and nucleic acid sequence of related Robo1 and Robo2 polypeptides. The specification further discloses that the claimed polypeptides can regulate cell function, especially nerve cell function and morphology and that the polypeptides may be either made recombinantly using the disclosed polynucleotide sequence or purified from mammalian cells. Also disclosed are isolated hybridization probes and primers capable of specific hybridization, methods of making and using the compositions in diagnosis, therapy and for making reagents, see in particular p. 3 lines 3-16. However, the specification appears to merely disclose a research plan for performing further experimentation aimed at the discovery of such real-world uses for the claimed sequences. For example, the specification fails to disclose any specific and substantial, credible regulation of cell function, change in morphology, disease to be diagnosed or therapy which is achieved. Thus the disclosed utilities appear to merely constitute research reagents which rely on the inherent properties of any nucleic acid to hybridize and encode. Further no evidence or art of record presents a well established utility for the claimed nucleotides. Thus, for the aforementioned reasons the claimed nucleic acids lack a defined specific and substantial, credible utility or a well established utility.

While the specification notes as taught by Seeger et al., Neuron 10(3):409-26, 1993 that Robo molecules are associated with neuronal midline crossing during a particular developmental stage, the specification and art fail to evidence how the claimed Robo molecules can be used to provide any benefit. Therefore applicants asserted "use" is not a specific and substantial utility because the artisan is un-apprised of the "real world use" or significance of marking Robo expression. Without an indication of how the discovered findings (directed to midline crossing) can be utilized to provide a specific and substantial benefit, utility is lacking. It is also noted that there is no evidence that any prior art disclosure of Robo or Robo-type molecules is sufficient to establish a well known utility for the claimed reagents.

Claims 68-91 and 93-119 are rejected under 35 U.S.C. 112, first paragraph. This rejection is set forth in the prior Office Action of 3-27-01, Paper No. 24. As set forth therein, since the claimed invention is not supported by either a specific and substantial, credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 81, 100, 102-103, 113-114 are rejected under 35 U.S.C. 112, first paragraph. This rejection is set forth in the prior Office Action of 3-27-01, Paper No. 24. As set forth therein, the isolated residues which do not appear to be specifically supported by the specification as originally filed are as follows; residues 1-942 of SEQ ID NO:4, and residues 1-284 of SEQ ID NO:10.

Claims 88-90 are rejected under 35 U.S.C. 102(a). This rejection is set forth in the prior Office Action of 3-27-01, Paper No. 24. O01632 and reference Wilson et al., of record correspond to U88183. U88183 teaches isolated polynucleotides encoding residues 424-1297 of SEQ ID NO:6. The examiner agrees that the original rejection was made over O01632. The "created date" of a GenEmbl sequence is the public availability date based upon information obtained from the USPTO biotech library and Genbank Embl. Thus, the public availability date was noted as 7-1-97, see record. Subsequently, applicants argued that Genbank also released Accession Nos. 1825710, 1825711 and U88183 which also contained residues 1-423 of instant SEQ ID NO:6. In the response received on 2-16-00 it is noted that applicants did indeed submit U88183 for consideration by the examiner. However such was not formally made of record on a PTO-1449. The copy provided to the examiner failed to note a "created date", the date the accession was created in the publicly available database. Therefore the record was obtained via the worldwide web by the examiner. The website is as follows; http://www.ebi.ac.uk/cgi-bin/emblfetch following arrival at this site U88183 was entered and the record was obtained. This duplicate record of U88183, originally provided by applicant is now subsequently provided to applicants for clarification and is cited on a PTO-892. The creation date noted on the record is 2-14-97. Thus, based on applicants arguments that the originally cited O01632 contains the same sequence as 1825710, 1825711 and U88183 provided by applicants, that the Accession No. of U88183 was created 2-14-97 and was publicly available on that date, and based on applicant's admission that U88183 is prior art and was publicly available from the Genbank database, this new Accession No. Provided by applicants was incoroporated into the prior art rejection, based

on applicant's admission. It appears only that the public availability dates of the Accession No is of issue. The attached copy of U88183 provides the creation date obtained by the examiner and is publicly reported as 2-14-97. Thus, the rejection is maintained.

Claims 94-95 are rejected under 35 U.S.C. 103(a). This rejection is set forth in the prior Office Action of 3-27-01, Paper No. 24. As set forth therein, Genbank Accession No:U88183 teaches consecutive residues of SEQ ID NO:6. However, U88183 does not teach the nucleic acids in a vector and host cell for the production of polypeptides as claimed in claims 94-95. The relative skill in the art is reflected by Sambrook et al which teach the expression of cloned DNA in mammalian cells using vector nucleic acids. Such vector and host cell materials were readily available, at the time of the invention. The skilled artisan is well apprised of such cloning techniques widely known in the art. It would have been prima facie obvious for one of skill in the art knowing the DNA of U88183, to clone U88183 into a vector and host cell using the techniques of Sambrook et al for the replication of the claimed nucleic acids, expression of the polypeptides, and sub-sequences thereof. One would have been motivated to clone such nucleic acids into a polypeptide expression vector in order to study the protein produced thereby from the cells. Further, one would have expected success based on the high skill in the art, the teachings of Sambrook et al and the public availability of numerous cell lines capable of expression. The knowledge of the appropriate DNA sequence taught by U88183 in the prior art renders the claimed nucleic acids, vectors, host cells and method of producing the polypeptides obvious.

(11) Response to Argument

With respect to 35 USC 101, Appellants argue at pp. 3-4 of the brief that the claims are drawn and limited to diagnostic probes useful to trace the presence of Robo expression in tissue; that the probes are as useful as any equipment or reagent used in commercial research, that the polynucleotides of claims 68-71, 73-74, 79-81, 83-84, 88-91, 94-95, 100-104, 106-107, 112-114, and 116-117 which encode polypeptides capable of eliciting a Robo specific antibody are useful as evidenced by their manufacture and sale as industrial commercial products; that the polynucleotides of claims 72, 78, 82, 87, 93, 99, 105, 111 and 115 are useful in the manufacture of the aforementioned Robo specific antibodies; and that the proteins regulate neural guidance and are important targets for therapeutic intervention.

In response, it is noted that the claims are not directed to diagnostic probes. As previously noted Appellants do not specify how the claimed invention is diagnostic in nature and do not teach the significance or utility of marking Robo expression in any particular patient or sample. Similarly, the use of the polynucleotides for producing peptides capable of producing Robo-specific antibodies similarly lacks utility for the aforementioned reasons previously of record. Sale and manufacture are not evidence sufficient to provide for utility absent a significant and substantial use for the noted reagents. Moreover, while the specification notes as taught by Seeger et al., Neuron 10(3):409-26, 1993 that Robo molecules are expressed during neuronal midline crossing at a particular developmental stage, the specification and art fail to evidence how marking or manipulating such expression can be used to provide specific and substantial benefit within the context of 35 USC 101. In particular while Robo proteins can regulate neural midline crossing during neuronal development, the artisan is

not apprised of how to use the claimed polynucleic acids, proteins encoded thereby, host cells comprising the nucleotides or antibodies generated by such to provide for any marking or manipulation which provides benefit or can be used as a target in a therapeutic invention as hypothetically asserted.

With respect to 35 USC 112, first paragraph, Appellants reiterate the arguments noted above at p. 5, II.

In response, the comments above are reiterated with respect to enablement.

With respect to claim 81 and 35 USC 112, first paragraph, Appellants argue at pp. 5-6, III, that the specification discloses the particular residues as in Table 1; that the specification teaches that the polypeptides of the invention include incomplete translates and deletion mutants of SEQ ID NO:4 (p. 4, lines 6-8); and that this defines a Robo (extracellular domain) taught to be advantageously targeted with monoclonal antibodies (p. 29, lines 16-17).

In response, these comments and the noted passages of the specification have been fully considered. However, Table 1 is an alignment of particular Robo amino acid sequences. The specification does not appear to support the specific polynucleotides encoding particular incomplete translates or deletion mutants as argued. It is noted that it is the polynucleotides which are recited in the claims. In particular, the generic concept of polynucleotides encoding incomplete translates or deletion mutants is not found. The noted passages and Table 1 considered together do not appear to support the specific polynucleotide embodiments claimed as of the filing date. It is noted that SEQ ID NO:4 is 1381 amino acid residues in length and that 1-942 of SEQ ID NO:4 is neither specifically identified as an extracellular domain, nor

does the specification appear to contemplate polynucleotides encoding the specific deletion of residues 943-1381.

With respect to claims 100, and 102-103 and the 35 USC 112, first paragraph rejection, Appellant's argue at p. 6 that the polypeptide of residues 68-259 of SEQ ID NO:8 are disclosed at p. 4, line 19 and note that the cited sequence does not appear in claims 100 and 102-103 so the claims are grouped separately.

In response, the comments and noted passages have been fully considered but are not persuasive with respect to claims 100 and 102-103. The recitation of residues 68-259 of SEQ ID NO:8 as argued are not noted in the claims. Moreover the polynucleotides encoding the specific residues as noted in claims 100 and 102-103 are not clearly supported by the specification as filed, or particularly by the passage at p. 4, line 19 as argued by Appellants.

With respect to claims 113-114, Appellants argue at p. 6 that the polypeptide of residues 1-284 of SEQ ID NO:10 were particularly disclosed in Table 1, that the alignment does not diminish the separate disclosure and that the incomplete translates and deletion mutations were contemplated at p. 4, lines 6-8. Appellants note that claim 113 does not recite the specific mutation addressed.

In response, these comments and the noted passages of the specification have been fully considered. However, Table 1 is an alignment of particular Robo amino acid sequences. The specification does not appear to support the polynucleotides encoding the specific incomplete translates or deletion mutants as recited in the claims. In particular, the generic concept of an

incomplete translate and Table 1 considered together do not appear to support the specific embodiment claimed as of the filing date, in particular to encoding polynucleotides or to the polynucleotides encoding the specific residues which are not noted in the specification as filed. It is noted that SEQ ID NO:10 is 434 residues and that the specification does not appear to specifically support the deletion of the residues 385-434 so as to provide for the recitations of the claims.

With respect to claims 88-90 and the 35 USC 102(a) rejection, Appellant's arguments are presented at pp. 6-7, IV. Appellants review particular sequence Accession numbers and their submission history as noted in the file. Appellants argue to the extent of 1825710 and '711 that the 1.131 Declaration obviates the rejection over these publications. Appellants argue with respect to U88183 that the creation date is the date the record was originally created and asserts that the reliance on such date is improper. Appellants refer to highlighted copies of database information and state that even the date of last modification may not correspond to the release date.

In response, the rejection of record does not pertain to the '710 and '711 sequences although they are noted in Appellants arguments as presented in the brief and in previous responses as noted by Appellants. Thus, the 1.131 Declaration is moot with respect to them is moot. Of issue is the public availability date of Genbank EMBL Accession No. U88183 which as published indicates the earliest date noted as the creation date of 2-14-1997. Appellants argue that the creation date is not the public availability date for this record. However, Appellants have placed no evidence on record to substantiate this allegation, nor have they

provided evidence as to what the proper publication date for the reference is. Appellants specifically refer to submission data regarding the "Modification Date" as provided by a sample record at www.ncbi.nlm.nih.gov. In the passage highlighted by Appellants the following is stated on the website pertaining to sequence records.

> The date in the LOCUS field is the date of last modification. In some cases, it might correspond to the release date, but there is no way to tell just by looking at the record. If you need to know the first date of public availability for a specific sequence record, send a message to info@ncbi.nllm.nih.gov. We will check the history of the record for you, and let you know the date of first public release. If the sequence was originally submitted to our collaborators at DDBJ or EMBL, rather than to GenBank, we will ask them to send the release date information to you.

This procedure is routine in the Patent Office to establish publication dates for sequence records. In this case, as previously noted the procedure resulted in a communication to the Office specifying that the public availability date for this record was prior to the April 1997 date of Appellant's declaration. As further evidenced by the published record of U88183 by Genbank, the earliest date noted on the reference is the created date reported by Genbank to be 2-14-97. This established public availability date was cited in the rejection of Paper No's. 24 and 29 and the record was provided to Appellants with the date on it. However, there is no evidence on record which establishes that Appellant performed this noted procedure to actually establish what the public availability date of the U88183 reference actually is or that it is after the relevant April, 1997 date of Appellant's declaration. However, this procedures was performed by the Examiner a second time after filing of the response to the 3-27-01 Action and a third time in response to the brief to assure that the first communication was not in error. The email communication string is appended herein to establish that the procedure referenced by Appellants was actually followed and that the date reported by GenBank as the public

availability date was prior to the relevant April 1997 date of Appellant's declaration as originally communicated to Appellants by the Examiner.

-----Original Message-----

From: mcginnis@ncbi.nlm.nih.gov [mailto:mcginnis@ncbi.nlm.nih.gov]

Sent: Wednesday, August 21, 2002 11:00 AM

To: Caryn.Wesner@uspto.gov

Cc: mcginnis@ncbi.nlm.nih.gov

Subject: EMBL dates needed

Hi;

Some of these sequences are Protein sequence. We only can give the date for ofrst release for the nucleotide sequence from whioch the proteins were derived.

I have attached some information below regarding the release date(s) of the GenBank accession number(s) about which you have inquired.

GenBank collaborates with the EMBL database in Europe and the DDBJ database in Japan to produce and distribute the International DNA Sequence Databases. The International DNA Sequence Databases take no responsibility for making any determination of the priority issues for patent claims. We are able only to inform you, to the best of our knowledge, of the release date of the pertinent sequence into the public database. We appreciate your understanding and cooperation.

1825710= AAB52657 = U88183.1

1825711= AAB52658 = U88183.1

U88183.1 First Public 2/7/1997

001632 is not a recognised NCBI Accession number and does not occur in GenBank or GenPept.

Sincerely,

Scott McGinnis, M.S.

National Center of Biotechnology Information.

HTTP://www.ncbi.nlm.nih.gov

---------- Begin Forwarded Message ----------

From: Caryn.Wesner@uspto.gov

To: info@ncbi.nlm.nih.gov

Subject: EMBL dates needed

Date: Wed, 21 Aug 2002 10:34:28 -0400

MIME-Version: 1.0

X-Virus-Scanned: by amavisd-milter (http://amavis.org/)

X-Virus-Scanned: by amavisd-milter (http://amavis.org/)

X-Filter-Version: 1.8 (mail-blade4)

X-Spam-Status: No, hits=1.2 required=5.5 tests=NO_REAL_NAME version=2.01

Please provide the dates of public availability for these Genbank/EMBL Accession numbers:

1825710

1825711

U88183

O01632

If you have any questions, please e-mail or call the number below. Thank you very much.

Caryn S. Wesner-Early, MSLS
Technical Information Specialist
Biotechnology and Chemical Library
U.S. Patent and Trademark Office
Phone: (703) 308-4501
Fax: (703) 308-4496
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---------- End Forwarded Message ----------

The above email evidences that the case presented to Appellants on the record as to the date of the U88183 reference is consistent with a public availability date prior to April 1997. The previously communicated reference as obtained via the GenBank website indicated in print that the creation date was 2-14-1997 and was prior to April 1997. GenBank has previously indicated and again has indicated as evidenced above that the U88183 record was publicly available prior to the April 1997 date to which Appellants refer in their 1.131 declaration. Appellants have further argued that there are procedures whereby an inventor may submit sequence to the GenBank database with an accompanying request to keep the references secret until the corresponding publication is published or until a date as specified to be released.

However, there is no evidence of record of the date that the sequence was actually transmitted to the database or for any request that the sequence be held undisclosed to the public pending a publication of a particular reference or other release procedure. Thus, there is no evidence to establish that the created date would not also be the public availability date. Because Appellant's arguments do not establish that the public availability dates of U88183 were after the April 1997 date of Appellant's declaration, and because the creation date as noted in the record obtained for U88183 and communications with the GenBank database regarding the public availability date of the reference indicate that the reference was publicly available prior to April 1997, the rejection is maintained.

With respect to claims 94-95 and the 35 USC 103(a) rejection, Appellant's argue that the GenBank Accession No. O01632 (U88183 upon which the action relies is not prior art as argued in the 102(a) rejection above.

In response, it is noted that the rejection is over the U88183 sequence which date is established via the cited reference, the USPTO Biotech library and GenBank inquiries by the Examiner. Thus, the rejection is maintained as the U88183 reference is prior art under 102(a).

Therefore, for the reasons set forth above, Appellant's arguments have been fully and carefully considered, but are not sufficient to rebut the prima facie case of lack of utility, written description, enablement and prior art and it is believed that the rejections should be sustained.

Respectfully submitted,

Sharon L. Turner
January 20, 2004

Conferees: Gary Kunz, SPE
Yvonne Eyler, SPE

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SUPERVISORY PATENT EXAMINER
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